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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

GUPTA, ANISH

ART UNIT PAPER NUMBER

1654

DATE MAILED: 04/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

09/998,780

Applicant(s)

WAINWRIGHT ET AL.

Examiner

Anish Gupta

Art Unit

1654

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 02 March 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☒ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on 02 March 2005. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.

6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 71, 72 and 80-83.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.

12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_

13. ☐ Other: \_\_\_\_\_.

Continuation of 11. does NOT place the application in condition for allowance because: As a note, the claims are rejected for the same reasons as set forth in the previous office action, even as amended by the after final amendment. The reasons for maintaining the rejection follow.

Applicants argue that the rejection of Levin in view of Rice does not provide the requisite motivation to support a prima facie case of obviousness. Applicants state Levin does not expressly disclose the use of endotoxin binding protein immobilized on solid support. Rice disclose the measurement of antibodies in a sample using antigen coated piezoelectric oscillator. This reference does not disclose the use of an endotoxin protein. Further, the reasoning for combining the references, a means of analysis that is inexpensive and unsophisticated and results are obtained rapidly and accurately, is "insufficient to provide the proper motivation to import selected pieces of Rice into Levin. The proper test is whether there exists some specific motivation or suggestion in Levin to modify Levin with the method of Rice." Finally, no reasonable expectation of success has been provided. Generalized assertion are insufficient to in establishing reasonable expectation of success. "Objective evidence must be provided that establishes at least some degree of predictability."

Applicants arguments have been reviewed but have not been found persuasive.

"To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP 2143. The primary references teaches a method of measuring endotoxin in a sample using the protein from the amoeba of horseshoe crab. The secondary reference provides a means of measuring using piezoelectric oscillator detection method which rapid accurate and objective in its measurement and is inexpensive. Thus, one would be motivated to use this piezoelectric oscillator means. This is proper motivation. It is wholly unclear where it is required that the motivation must be "specific motivation or suggestion." Applicants, have simply met their burden in establishing why this is not proper motivation. Next, there is reasonable expectation of success because, as stated in the previous office action, the interaction between the protein from the Limulus polyphemus and endotoxin is similar to an antibody/antigen relationship. Rice teaches that means of conjugating proteins to the oscillator is conventionally known in the art. Thus, one would know how to conjugate the endotoxin protein to the oscillator. Since the interaction between the protein from the Limulus polyphemus and endotoxin is similar to an antibody/antigen relationship, which Applicants have not refuted, one would expect once the Limulus polyphemus protein is bound to the quartz oscillator, to interact with the endotoxin thereby changing the mass of the electrode and changing the frequency of the crystal. Thus, there is reasonable expectation of success. Finally as indicated in the previous office action all of the claimed limitation are disclosed when the primary reference and the secondary references are combined.

Rejection is maintained.

For Levin in view of Olivera, Applicants argue there is no motivation to combine the references. "Even assuming the Examiner's assertion are true for argument purposes, it is improper to import the teachings of Oliveira into Levin, because Levin fails to disclose, teach or suggest the use of a solid support to immobilize a protein."

Applicants arguments have been reviewed but have not been found persuasive.

A proper obviousness rejection does not require that each and every element be disclosed in primary reference. For example, in In re Linter the claimed invention was a laundry composition consisting essentially of a dispersant, cationic fabric softener, sugar, sequestering phosphate, and brightener in specified proportions. The claims were rejected over the combination of a primary reference which taught all the claim limitations except for the presence of sugar (emphasis added). Even though the primary reference did not disclose the use of sugar, the rejection was upheld because the secondary references taught the addition of sugar as a filler or weighting agent in compositions containing cationic fabric softeners. Thus, so long as the secondary reference provides motivation and a reasonable expectation of success, a proper rejection has been established.

Here, proper motivation and reasonable expectation of success has been established (see Final office action). The interaction between the protein from the Limulus polyphemus and endotoxin is similar to an antibody/antigen relationship. That is, the protein from the Limulus polyphemus binds with the endotoxin. Note that primary reference states that the protein from Limulus polyphemus reacts with the endotoxin in a sample resulting in an increase in turbidity or viscosity (see col. 3, lines 1-15 and claim 1). Further, Applicant's specification acknowledges this interaction, on page 3 of the specification, where it is taught the interaction between the Limulus polyphemus protein and endotoxin result in clot formation. Furthermore, Olivera et al. states that the method disclosed can be used for analysis of a variety of antigenic materials ranging from low molecular weight to compounds to large macromolecules (see col. 3, lines 36-40). Thus, one would expect, once the Limulus polyphemus protein is bound to the quartz oscillator, to interact with the endotoxin thereby resulting downward shift in the frequency of the oscillator. Note that Levin et al. teach the Limulus polyphemus protein can detect as little as five ten thousandths microgram of endotoxin per milliliter and thus is an effective means of measuring endotoxin.

Rejection is maintained..

  
ANISH GUPTA  
PATENT EXAMINER